REMARKS

Claims 1, 5, 7-9, and 11-37 are pending in the present application. By this Amendment, the specification is amended to correct a typographical error, claims 2-4, 6, and 10 are cancelled, claims 1, 5, and 32-34 are amended, and new claims 36 and 37 are added. Claim 1 is amended to incorporate the limitations of cancelled claim 6. Claims 5 and 33 are amended to correct the dependencies of these claims. Support for the amendments to claims 5, 32, and 34, and for new claims 36 and 37, can be found in the present specification at p, 7, lines 6-13. No new matter is added by this Amendment.

A. §103(a) Rejection over Shimizu in view of Sherwood

Claims 1-20 and 22-34 are rejected under 35 U.S.C. §103(a) as being obvious over Shimizu (U.S. Patent No. 6,328,994 B1 to Shimizu et al.) in view of Sherwood (U.S. Patent No. 5,585,115 to Sherwood et al.). This rejection is respectfully traversed.

Shimizu relates to an orally disintegratable tablet comprised of fine enteric-coated granules dispersed in an orally disintegrating mixture. The disintegrating mixture typically contains a water-soluble sugar alcohol which provides strength "and sufficient disintegration or dissolution in the oral cavity." (See Shimizu col. 9, line 49 *et seq.* and col. 10, lines 5-6.) The disintegrating mixture may also contain a binder especially crystalline cellulose (or "MCC") because MCC "provides a solid preparation which exhibits more excellent strength [ ] while retaining excellent disintegration and dissolution in the oral cavity." The amount of MCC binder, however, used in Shimizu is significantly less than the amount of silicified MCC required by instant claim 1.

In particular, Shimizu discloses that the crystalline cellulose is used "in an amount of about 3 to 50 weight %, preferably about 5 to 40 weight %, more preferably about 5 to

20 weight % relative to 100 weight % of the orally disintegrable tablet *apart from the fine granules*" (col. 10, lines 25-29 (emphasis added)). That is, the maximum 50% MCC disclosed by Shimizu does not relate to the total weight of the tablet. The weight of the fine granules is excluded from Shimizu's percentage. Accordingly, unlike the presently claimed invention, Shimizu uses significantly less than 50% of a microcrystalline cellulose-type binder.

Additionally, Shimizu is a relatively slow orally disintegrating tablet. While generically teaching a preferred oral disintegration time (measured in the adult mouth and not *in vitro* as per the present invention) of "more preferably about 30 seconds or less," the fastest example achieves oral disintegration in 20 seconds. (See col. 12, lines 42-47 and Example 4.)

Recognizing that Shimizu does not teach or suggest using the Applicant's claimed silicified MCC, the Examiner's rejection relies upon Sherwood. This proposed combination of teachings, however, fails to construct the claimed invention or otherwise render it obvious.

Most notably, nothing in Shimizu or Sherwood would suggest the use of the Applicant's claimed at least 50 wt.% of silicified MCC. Replacing the MCC in Shimizu with silicified MCC, which the Examiner's purports to have been obvious, would result in too little silicified MCC in order to meet Applicant's claim 1. The fact that Sherwood teaches tablets having greater amounts of silicified MCC is irrelevant because those tablets are not orally disintegrating. Indeed, Shimizu uses a water-soluble sugar as the basic agent for achieving oral disintegration; a generally known prior art concept for seeking oral disintegration (See page 2, lines 5-11 of the present specification.) And

Shimizu describes the water-soluble sugar as providing the oral disintegration whereas the MCC binder is described as not interfering with such functionality. Increasing the amount of binder and decreasing the amount of water-soluble sugar, either Shimizu's MCC or as modified by Sherwood with silicified MCC, would have been expected to adversely affect the orally disintegratabiliy of the tablet. Accordingly, there is no motivation to combine the teachings of Shimizu and Sherwood to obtain the Applicant's claimed orally disintegrating tablet containing at least 50 wt.% of silicified MCC.

Moreover, Shimizu and Sherwood do not provide a reasonable expectation of achieving the Applicant's disintegration time of 1-15 seconds. Note that Shimizu's measured disintegration is based on an oral administration. As explained on page 6 of the present specification, generally the *in vitro* disintegration test times are somewhat longer than the orally experienced time for disintegration. Shimizu's tablets if tested in the Applicant's defining *in vitro* disintegration test would likely yield slightly longer times than as reported in Shimizu e.g., longer than 20 seconds. Nothing in Shimizu or Sherwood teaches the reader how to improve these disintegration times. And certainly nothing in Sherwood teaches or suggests that silicified microcrystalline cellulose would be useful in improving oral disintegration times.

Accordingly, given that Shimizu teaches the use of lower amounts of MCC binder and longer disintegration times and given that Sherwood fails to teach the use of silicified MCC as an oral disintegrating agent, it could not have been obvious to the worker or ordinary skill in the art to change the MCC binder in Shimizu to silicified MCC, increase the amount of the binder, and have a reasonable expectation of achieving the Applicant's

claimed disintegration times. Therefore, the presently claimed subject matter is unobvious over the combination of Shimizu and Sherwood.

B. §103(a) Rejection over Betzing in view of Shimizu and Sherwood

Claims 1-35 are rejected under 35 U.S.C §103(a) as being obvious over Betzing (U.S. Patent No. 5,776,492 to Betzing et al.) in view of Shimizu and Sherwood. This rejection is respectfully traversed.

Betzing teaches rapidly disintegrating tablets comprising MCC. The tablets, however, disintegrate significantly slower than the presently claimed orally disintegrating tablets. As shown in the Table in column 5 of Betzing, the fastest tablets disintegrated in 25-30 seconds. Other Betzing inventive tablets disintegrated in the 100-110 second range. This is not too surprising given that Betzing intends to form a suspension of the disintegrated tablet in a liquid prior to administration (See col. 2, lines 61-65). While one to two minutes is sufficiently rapid for a tablet to disintegrate in a glass of water before drinking, such lag time is not desired in an orally disintegrating tablet that may be placed directly into the mouth.

The Examiner's rejection proposes to overcome the deficiencies in Betzing by reliance on the teachings of Sherwood and Shimizu. But this combination of teachings does not suggest the formation of the presently claimed invention.

A worker of ordinary skill in the art would not have found it obvious to modify the MCC called for in Betzing with the silicified MCC of Sherwood. Betzing indicates the importance of the particular excipient combination in several places. At column 3, lines 20-28, Betzing indicates that replacement of MCC with either a water soluble

lactose (a sugar) or a water insoluble calcium hydrogen phosphate results in a significant decrease in the disintegration rate (see also comparative Examples 6 and 7). That a water soluble sugar produces a slower disintegration rate is counter-intuitive. That a water insoluble excipient such as calcium hydrogen phosphate also decreased the disintegration rate counsels against the use of silicified MCC; an MCC that further contains the water insoluble excipient silicon dioxide. Moreover, Betzing indicates that a certain amount of starch is useful in stabilizing disintegration times over a variety of tablet hardness (See col. 3, lines 7-19). But too much starch/not enough MCC can actually decrease disintegration times (col. 3, lines 22-25). The impression given the reader is that these precise excipients in specific ratios must be used and thus the replacement of MCC with silicified MCC would at best yield uncertain results and more likely would be expected to further slow the disintegration.

Additionally, as discussed in the previous rejection, there is no teaching in any of the applied patents of obtaining an orally disintegrating tablet meeting the Applicant's claimed 1-15 seconds. Accordingly, there is no reasonable expectation of success in replacing the MCC of Betzing with the silicified MCC of Sherwood to obtain the Applicant's claimed fast disintegration time of 1-15 seconds.

For at least these two reasons, the formation of the presently claimed invention could not have been obvious to a worker of ordinary skill of the art at the time the present invention was made.

C. Conclusion

In view of the foregoing amendments and remarks, the present claims define novel, patentable subject matter. Reconsideration of the rejections and allowance of the present application are respectfully requested.

Should the Examiner have any questions regarding this application, she is encouraged to contact Mark R. Buscher (Reg. No. 35,006) at telephone No. 703 753 5256.

Respectfully submitted,

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